(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 609 914 A2**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **94105150.0**

(51) Int. Cl.⁵: **A61M 25/10, A61M 1/10**

(22) Date of filing: **26.01.87**

Diese Anmeldung ist am 31 - 03 - 1994 als Teilanmeldung zu der unter INID-Kode 60 erwähnten Anmeldung eingereicht worden.

(30) Priority: **31.01.86 US 824721**

(43) Date of publication of application: **10.08.94 Bulletin 94/32**

(60) Publication number of the earlier application in accordance with Art.76 EPC: **0 402 964**

(84) Designated Contracting States: **AT DE FR GB IT**

(71) Applicant: **Mohl, Werner, M.D.**
Endemanngasse 6-18/2/35
Flat 235
A-1238 Vienna(AT)

(72) Inventor: **Mohl, Werner, M.D.**
Endemanngasse 6-18/2/35
Flat 235
A-1238 Vienna(AT)

(74) Representative: **Altenburg, Udo, Dipl.-Phys. et al**
Patent- und Rechtsanwälte
Bardehle . Pagenberg . Dost . Altenburg . Frohwitter . Geissler & Partner
Postfach 86 06 20
D-81633 München (DE)

(54) **Pressure-controlled intermittent coronary sinus occlusion.**

(57) The coronary sinus is intermittently occluded by use of means for occluding the sinus, a pressure transducer (50) for sensing the fluid pressure signals, and a controller (28) responsive to the transducer and arranged to provide trigger signals to the occluding means to trigger an occlusion and to interrupt the occlusion, the system being characterized in that the controller is arranged to estimate a plateau level of the fluid pressure during each conclusion and for providing a trigger signal to interrupt each conclusion on the basis of the estimate. The duration of the interruption before the next occlusion is controlled in response to the volume flow in the sinus during the interruption. Pharmacological agents are injected into the heart tissue. A analysis of heart function is obtained by analyzing the local pressure maxima in successive heartbeats during occlusion. Initiation of the next occlusion is timed based on fluid pressure signals taken from the sinus during occlusion.

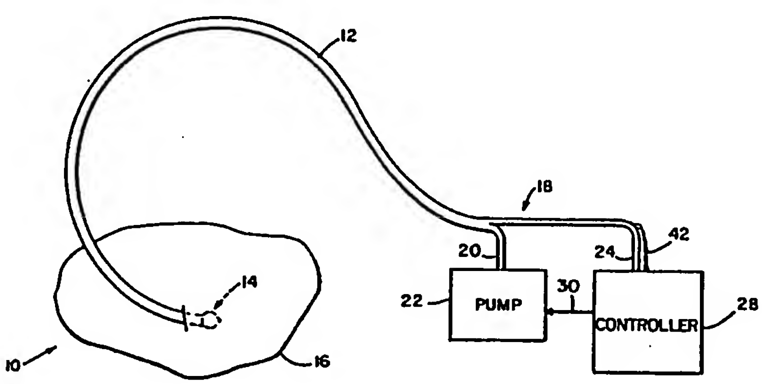


FIG. 1

EP 0 609 914 A2

This invention relates to intermittent periodic occlusion of the coronary sinus in order to accomplish the major vein which collects blood from the heart muscle in order to cause venous blood to flow back from the normal contracting myocardium to reach ischemic portions of the heart muscle.

Arterial blood which feeds the heart muscle is able to pass through and nourish healthy heart tissue, but has difficulty in reaching the ischemic tissue. This reduces the delivery of nutrients to, and the carrying away of the waste products of metabolism (metabolites) from, the ischemic tissue.

It has been proposed to reach the ischemic tissue by causing blood to flow in a reverse direction from the coronary sinus back through the coronary venous system. Such retroperfusion has been attempted by feeding blood into the coronary sinus from another source, either by permanently connecting an artery to the coronary sinus or by temporarily inserting into the sinus a catheter supplied with blood which has been taken from a remote artery and passed through a blood pump outside the patient's body.

Another proposed technique for retroperfusion uses an inflatable balloon held on the end of a catheter to intermittently occlude the coronary sinus. Blood pressure in the sinus then rises as the heart beats so that blood received in the sinus through the healthy tissue of the heart muscle is forced back into the ischemic tissue. In such intermittent coronary sinus occlusion, the balloon end of the catheter is inserted percutaneously or intraoperatively. The other end of the catheter is supplied with gas or liquid by a pump which can be controlled to cause the balloon to inflate and deflate cyclically, for example at a rate synchronized with the heart pulse rate, or on the basis of pressure.

In general, the invention concerns an improvement that leads to making intermittent occlusion of a coronary sinus a successful and useful technique. The invention employs means for occluding the sinus, a pressure transducer for sensing the fluid pressure within the sinus and providing corresponding fluid pressure signals, and a controller responsive to the transducer and arranged to provide trigger signals to the occluding means to trigger an occlusion and to interrupt the occlusion. In one aspect, the invention is characterized in that the controller is arranged to estimate a plateau level of the fluid pressure during each occlusion and to provide the trigger signals to interrupt each occlusion on the basis of said estimate. The controller is also arranged to calculate the optimum deflation time between occlusions utilizing data obtained from coronary sinus blood pressure and/or flow.

The invention is found to provide sufficient retroperfusion flow to effectively wash toxic metabolites and edema from the ischemic tissue while minimizing damage to healthy tissue. Heart contractability can be improved. The invention may be used in bolstering heart function during heart surgery and catheterization, especially in combination with conventional pharmacological agents.

In preferred embodiments, each occlusion is interrupted before the fluid pressure reaches the plateau level; the plateau value is estimated in real time during each period of occlusion based on exponential curve fitting; the controller includes sampling circuitry for sensing the fluid pressure signals, e.g., by storing the sensed signals at a rate substantially higher than the heartbeat rate, first analysis circuitry for determining and storing a local maximum value of the pressure for each heartbeat from the stored sensed signals, second analysis circuitry for estimating in real time the plateau level from the stored local maximum values, and comparison circuitry for comparing a predetermined percentage of the estimated plateau level with successive local maximum values, and generating trigger signals for triggering interruption of each occlusion at a time dependent on the result of the comparison; the predetermined percentage is calculated from a range of 70-98%, or a calculated value thereof of X% + n (n = heart cycles or time), preferably 94%; and the occluding means includes an inflatable element in the sinus, and a pump for selectably inflating the inflatable element.

In another aspect, the invention features use of a sensor for delivering flow signals indicative of the volume flow of fluid in the sinus during periods when the occlusion is being interrupted, and the controller is arranged to trigger the initiation of the next occlusion at a time determined by the flow signals. The desirable effects of retroperfusion and washout thus can be optimized consistent with maintaining adequate coronary arterial flow.

In preferred embodiments, the flow signals represent velocity of flow, or fluid pressure as a function of time; the point at which to restart occlusion is accurately determined in real time during each period of interruption; the controller employed includes sampling circuitry for sampling the flow signals and storing the samples, analysis circuitry for determining from the stored samples the time when the peak of the flow occurs during each period of interruption of the occlusion, and trigger circuitry for delivering a trigger signal to trigger the next occlusion at a time determined by when the peak occurs; and the time of start of occlusion is after the occurrence of maximum flow in the coronary sinus.

In another aspect, the invention features recording and displaying the pressure maxima for the succession of heartbeats that occur during an occlusion to permit evaluation, e.g., in real time, of their relationship for indication of the state of health of the heart tissue. It is realized, for instance, that the rate of

rise of the curve of maxima usually indicates the contractility of the heart, the steeper the rate of rise, the more contractile.

In another aspect, the invention features means, during the occlusion, for infusing a pharmacological agent into the sinus whereby the agent can be retroperfused to the heart tissue. In this manner cardioplegic and thrombolytic agents can reach ischemic tissue, e.g., during heart surgery.

In another aspect, the invention features a method for aiding analysis of heart function which includes the steps of occluding the coronary sinus, measuring the fluid pressure in the sinus, plotting the fluid pressure against time during the occlusion, and analyzing the successive local pressure maxima which occur in successive heartbeats during the occlusion.

In another aspect, the invention features triggering the initiation of the next occlusion at a time based on fluid pressure signals taken from the sinus during occlusion. As a result, the start of the next occlusion can be delayed until the time when peak reactive hyperemia has occured.

In preferred embodiments, the timing of the initiation of the next occlusion is based on a combination of parameters derived from successive pressure maxima and pressure minima. The pressure maxima and minima are fitted to exponential curves. The parameters include heart rate, the asymptotic plateaus of the exponential curves, and the time constants of the exponential curves.

We first briefly describe the drawings.

Fig. 1	is a diagrammatic view of a heart with intermittent coronary sinus occlusion apparatus.
Fig. 1A	is a flowchart associated with the operation of the intermittent coronary sinus occlusion apparatus of Fig. 1.
Fig. 2A	is an isometric view broken away, of the distal end of the catheter of Fig. 1.
Fig. 2B	is an isometric view of an alternative embodiment of Fig. 2A.
Fig. 3	is a block diagram of the controller of Fig. 1.
Figs. 4, 7	is a representational graph of changes of coronary sinus pressure with time.
Fig. 5	is a representational graph of changes of coronary sinus pressure with time showing the interrupt period.
Fig. 6	is a representational graph of changes or coronary blood flow rate with time.
Figs. 8	through 16 are graphs of normalized data points of various parameters versus the time of peak reactive hyperemia (Tp).
Fig. 17	is a graph of data points of predicted Tp versus measured Tp.
Fig. 18	is a flow chart of a procedure for triggering start of occlusion.
Fig. 19	is a block diagram of apparatus for performing the procedure of Fig. 18.

Referring to Fig. 1, intermittent coronary sinus occlusion apparatus 10 includes multi-lumen catheter 12 having its distal end 14 inserted into the coronary sinus of heart 16 via the right atrium. The proximal end 18 of catheter 12 has a balloon inflation lumen 20 connected to pump 22. A second lumen 24, coaxial with lumen 20, and wires 42 are connected to controller 28 which contains circuitry for delivering control signals over line 30 to trigger the starting and stopping of pump 22.

Referring to Fig. 2A, at distal end 14 of catheter 12, lumen 20 communicates with inflatable balloon 34 via proximal aperture 32. Lumen 24 passes through the balloon and exits distally via aperture 36. Lumen 20 and balloon 34 contain gas delivered from pump 22.

The distal end of lumen 24 is open to the coronary sinus and holds a stationary column of isotonic heparinized saline solution with or without pharmacological agents. Changes in blood pressure in the sinus are transmitted to the proximal end of lumen 24, and are sensed at controller 28. (Pressure may also be sensed by fiberoptic elements residing in lumen 24.)

The distal end of lumen 24 is surrounded by an ultrasonic transducer 40 for sensing the flow of fluid in the sinus and delivering corresponding flow signals. Transducer 40 is connected to wires 42.

Referring to Fig. 2B, the catheter may include a third lumen 65 for carrying cardioplegic and thrombolytic (or other pharmacological) agents into the sinus for retroperfusion to the ischemic tissue. The delivery of the agents through lumen 65 may begin as soon as the balloon is inflated of may be triggered based on the trend of the local maxima during infusion.

Referring to Fig. 3, controller 28 has a pressure transducer (or other pressure sensor) 50 attached to the proximal end of lumen 24 (for sensing the blood pressure in the coronary sinus and providing corresponding fluid pressure signals). Transducer 50 is connected through amplifier 52 and interface 54 (which includes an A-to-D converter) to processor 56.

Processor 56 has microprocessor 58, RAM 60, and ROM 62 (which holds the program for processor 56). Processor 56 also has an input connected to flow analyzer 63, which includes Doppler circuitry for driving transducer 40 to vibrate ultrasonically and for detecting the Doppler shift of the resulting vibrationos bouncing back to transducer 40 from blood flowing in the coronary sinus, thus to give an indication of flow

velocity.

The output of processor 56 is connected through interface 64 (including a D-to-A converter) to line 30 which carries trigger signals to turn on and shut off pump 22.

Processor 56 is also connected to real time display 83 for displaying the sinus pressure over time for observation of the successive local pressure maxima as an indication of the state of health of the heart tissue, e.g., its contractility.

The distal end of catheter 12 is inserted, percutaneously or intraoperatively, into the coronary sinus. In operation, controller 56 issues a trigger signal through interface 64 and over line 30 to turn on pump 22. Gas is pumped into lumen 20 causing balloon 34 to inflate within the coronary sinus, blocking blood flow out of the sinus. Blood continues to flow into the sinus and retroperfuses back into the ischemic tissue.

Referring to Fig. 4, with the sinus blocked, systolic pressure 67 varies cyclically with the heart pulse rate. For each heartbeat, pressure rises to a local maximum (e.g., 68), and then falls near to a base level, after which the cycle is repeated. The successive local maxima lie on a curve 70 which rises toward asymptotic plateau 72, e.g., 108,8 g/cm^2 (80 mm Hg). With higher pressures, the retroperfused blood reaches more ischemic tissue, but the peak pressure for successive heartbeats rises approximately exponentially and we realize, accordingly, that the amount of additional tissue being reached in each successive heartbeat is not as great as in prior heartbeats. We also realize that a benefit of retroperfusion, the washout of metabolites, is dependent upon atttainment of pressure, but not prolongation of pressure, at the ischemic site, while continuing to occlue the sinus once plateau 72 is reached could damage healthy heart tissue. According to the invention, controller 28 is arranged to terminate the occlusion on the basis of the predicted plateau, more specifically when the sinus pressure reaches a predetermined level (e.g., 94% of the predicted plateau, or a calculated value thereof (i.e., X% (70-98%) of predicted plateau and n heart cycles or X% and n seconds)).

Referring to Fig. 1A, processor 56 samples (0) the output of interface 54 many times in each heart pulse cycle (e.g., at a rate of at least 2500 Hz) and stores the pressure samples in RAM 60. It then compares successive samples to determine the local maximum pressure for each heartbeat. Each local maximum is stored (84) in RAM 60. Processor 56 then performs a curve fitting route (86), e.g., by regression analysis, in which the available local maxima are fitted to an exponential function of the form $P = A - Be^{-ct}$, where P is the pressure as a function of time, A is the plateau pressure, t is time and B the difference between the plateau and the base-line pressures, and c is the slope contant. From the resulting function, processor 56 estimates (88) the level that plateau 72 would have and calculates 94% of that plateau (89). Finally, processor 56 compares (90) each newly calculated local maximum with the 94% value and when a local maximum first reaches at least that 94% value (e.g., at time 92 in Fig. 4), processor 56 triggers the pump to evacuate, or provide negative pressure to, lumen 20, thus interrupting the inflation of balloon 34 before the plateau is reached.

The local maxima can also be displayed in real time 85 in order to permit analysis of the condition of the heart tissue, and can be used as the basis for triggering an infusion of pharmacological agents 87.

Referring to Fig. 5, after pump cutoff, the curve of the local pressure maxima falls off to its baseline level until, at time 100, the pump is turned on again and the cycle repeats.

During occlusion, the heart muscle vascular system is subjected to back pressure and accordingly is resiliently expanded. When pump 22 is shut off and the back pressure is relieved, the heart muscle resiliently relaxes by contracting, thus forcing blood, toxic metabolites, and water from the ischemic tissue into the coronary sinus and other drainage systems, i.e., the besian vessels and lymph vessels.

How long the pump operation should be interrupted before initiating a subsequent occlusion depends on balancing the effect of maximum out-washing obtained by a longer interruption period with the effects of additional retroperfusion obtained by a shorter interruption period.

Referring to Fig. 6, the flow rate of blood in the sinus after occlusion has stopped rises exponentially to a peak value 102. By allowing the pump interruption to last at least until peak 102 is reached, the desirable effects of the intermittent occlusion can be optimized.

Referring again to Fig. 1A, this is accomplished by having processor 56 sample (104) the flow velocity signals delivered from flow analyzer 63, performing a curve fitting (106) of the samples to an exponential curve to determine (107) the peak flow 102, and triggering pump turn-on time (108) to occur after a predetermined brief period following the peak.

Other flow sensors can be used such as those which measure the resistance of a thermistor driven by a regulated current, as the sinus blood flows past the termistor. Alternatively, rather than measuring flow velocity, the flow volume in the sinus may be determined inferentially from the detailed sampling of sinus pressure with time (particularly during the period of a single heartbeat), using appropriate correlation analysis (105), as shown in Fig. 1A.

Alternatively, rather than measuring either flow velocity or flow volume, the time to begin occlusion (i.e., the time T, of peak reactive hyperemia corresponding to point 102 on Fig. 6) can be determined by measuring certain characteristics of the coronary sinus pressure curve, CSP(t), during the previous period of occlusion. Referring to Fig. 7, a typical plot of coronary sinus pressure against time, beginning at the onset of occlusion (t_0), exhibits a series of systolic pressure peaks 110 interleaved with a series of diastolic valleys 112. The pulse period 114 of the heartbeat is represented by the time between successive peaks or between successive valleys. The systolic pressure peaks can be fitted to an exponential curve 116 of the form $P_s(t) = (A_s(1-3^{-t/T}s)$ where $A_s$is the asymptotic plateau of pressure maxima and T_s is the time tp reach the plateau. Similarly the diastolic pressure valleys can be fitted to an exponential curve 118 of the form P_d-(t) = $A_d(1-3^{-t/T}d)$ where A_d is the asymptotic plateau of diastolic pressure valleys, and T_d is the time to reach the plateau. T_p represents the period between the termination of occlusion and the peak reactive hyperemia. T_p can be estimated as

$$\begin{aligned} T_p \;=\; & -\; 1{,}60\ T_s + 0{,}82\ T_d + 3{,}70\ T_s/T_d \\ & -\; 3{,}50\ T_d/T_s - 0{,}260\ A_s + 1{,}60\ A_d \\ & -\; 0{,}510\ A_s/A_d - 53{,}0\ A_d/A_s \\ & -\; 0{,}0081\ HR + 18{,}0\ RRI + 0{,}65\ A_s/RRI \\ & -\; 0{,}38\ A_d/RRI - 0{,}10\ T_s/RRI + 0{,}15\ T_d/RRI + 7{,}7 \end{aligned}$$

where HR is the heart rate, i.e., the reciprocal of the pulse period, and RRI is the reciprocal of the heart rate.

Figs. 8-16 show the experimentally determined relationships between normalized T_p and normalized values of HR, T_s, T_s/T_d, T_d, T_d/T_s, A_s, A_d/A_s, A_d, and A_s/A_d in experiments with 12 dogs. The correlations represented by this data are

T_s = -.21	T_p + .49;	r = .11
T_d = -.39	T_p + 5,0;	r = .21
T_s/T_d = 0.63	T_p + .98;	r = .14
T_d/T_s = -.060	T_p + 1.1;	r = .18
A_s = 0.46	T_p + 62;	r = .003
A_d = -.041	T_p + 14;	r = .008
A_s/A_d = -.074	T_p + 5.1;	r = .046
A_d/A_s = .0002	T_p + .22;	r = .002
HR = -.419	T_p + 127;	r = .21

Fig. 17 shows the correlation between predicted $\hat{T}_p$ and measured T_p in seconds. A linear regression between $\hat{T}_p$ and T_p yields.

$\hat{T}_p$ = 0,92 T_p + 0,00; r = 0,634 (P 0,001)

Measured T_p had a mean of 3,4 seconds (SD = 0,9, n = 128).

Referring to Fig. 18, the steps for triggering the start of occlusion include sensing sinus pressure 150, determining local systolic peaks (maxima) and diastolic valleys (minima) 152, storing the maxima and minima 154, determining heart rate 156, fitting the stored data to exponential curves 158, predicting T_p 160, and deciding pump turn-on time 162 accordingly.

Referring to Fig. 19, the procedure of Fig. 18 is performed in the apparatus 170. Line 24 is connected to a pressure transducer 171 which detects the electrical signals representing coronary sinus pressure and delivers them to an amplifier 172 which in turn sends them to an A-to-D converter 174 which provides them to sample storage 176. A local max and min calculator 178 uses the stored samples to determine the local systolic maxima and diastolic minima and provides them to max and min storage 180. A heart rate calculator 181 uses the successive maximum to determine the heart rate HR which is delivered to parameter storage 182. A curve fitting calculator 184 simultaneously fits the stored max and min values to

exponential curves and generates the values A_s, A_d, T_s, T_d and delivers them to parameter storage 182. $\hat{T}_p$ calculator 186 then calculates $\hat{T}_p$ from the stored parameters and delivers its value to a pump turn-on trigger 188. Trigger 188 triggers pump turn-on at a time corresponding to the value $\hat{T}_p$.

Other parameters may also be used as the basis for timing the start of occlusion. For example, the frequency spectrum of the coronary sinus pressure curve during occlusion is also useful in determining $\hat{T}_p$. For this purpose the $\hat{T}_p$ calculator 186 in Fig. 19 can be arranged to perform the appropriate Fourier analysis of the CSP data to derive a frequency spectrum, and to use the spectral information as one factor in calculating $\hat{T}_p$.

Claims

1. Apparatus (10) for intermittently occluding a coronary sinus comprising
   means for occluding said sinus,
   a pressure transducer (50) for sensing the fluid pressure within said sinus and providing corresponding fluid pressure signals, and
   a controller (28) responsive to said transducer having means for providing trigger signals to said occluding means to trigger an occlusion and to interrupt said occlusion, said apparatus being characterized in that
   said controller includes means (88) to estimate a plateau level (72) of said fluid pressure during each occlusion and means (56) to provide the trigger signal to interrupt each said occlusion on the basis of said estimate.

2. The apparatus of claim 1, further characterized in that each said occlusion is interrupted before said fluid pressure reaches said plateau level.

3. The apparatus of claim 1 further characterized by said controller comprising
   sensing circuitry (80) for sensing said fluid pressure signals,
   first analysis circuitry (82, 84) for determining and storing a local maximum value of said pressure for each heartbeat from said stored sensed signals,
   second analysis circuitry (88) for estimating in real time said plateau level from said stored local maximum values, and
   comparison circuitry (90) for comparing a predetermined percentage of said estimated plateau level with successive said local maximum values and generating said trigger signals for triggering interruption of each occlusion at a time dependent on the result of said comparison.

4. The apparatus of claim 2 or 3 further characterized by said predetermined percentage calculated from a range of 70-98% or a calculated value thereof of x% + n (n = heart cycles or time).

5. The apparatus of claim 4 further characterized by said predetermined percentage being about 94%.

6. The apparatus of claim 3 wherein said second analysis circuitry includes means (86) for estimating said plateau level by fitting said stored local maximum values to an exponential curve.

7. The apparatus of claim 1 further characterized in that said occluding means comprises an inflatable element (20) in said sinus, and a pump (22) for selectably inflating said inflatable element in response to said trigger signals.

8. The apparatus of claim 1 further characterized in having means (63) responsive to the volume flow in said sinus for commencing each period of occlusion of said sinus.

9. The apparatus of claim 1 further characterized in having means (83) to display the pressure maxima for the succession of heartbeats that occurs during an occlusion to enable evaluation of the relationship of said maxima for indication of the state of health of the heart tissue.

10. The apparatus of claim 1 further characterized in having means during said occlusion to infuse a pharmacological agent into said sinus, whereby said agent can be retroperfused to heart tissue.

11. Apparatus for intermittently occluding a coronary sinus comprising
    means for occluding said sinus, and
    a controller having means for providing trigger signals to said occluding means to trigger an occlusion and to interrupt said occlusion,
    said apparatus being characterized in that a sensor (104) is provided for delivering flow signals indicative of the volume flow of fluid in said sinus during periods when said occlusion is being interrupted, and
    said controller is arranged to trigger (108) the initiation of the next said occlusion at a time determined by said flow signals.

12. The apparatus of claim 11 characterized in that said flow signals represent the velocity of flow of fluid in said sinus.

13. The apparatus of claim 11, wherein said sensor comprises means for determining said flow signals based on the fluid pressure in said sinus as a function of time.

14. The apparatus of claim 11 further characterized in that said controller includes
    sampling circuitry for sampling said flow signals and storing said samples,
    analysis circuitry for determining from said stored samples the time when the peak of said volume flow occurs during each period of interruption of said occlusion, and
    trigger circuitry for delivering a trigger signal to trigger the next said occlusion at a time determined by when said peak occurs.

15. The apparatus of claim 14 wherein said trigger circuitry further comprises means for delivering said trigger signal to trigger said next occlusion after said peak occurs.

16. The apparatus of claim 11 further characterized in that said occluding means comprises an inflatable element (20) in said sinus and a pump for selectably inflating said inflatable element in response to said trigger circuitry.

FIG. 1

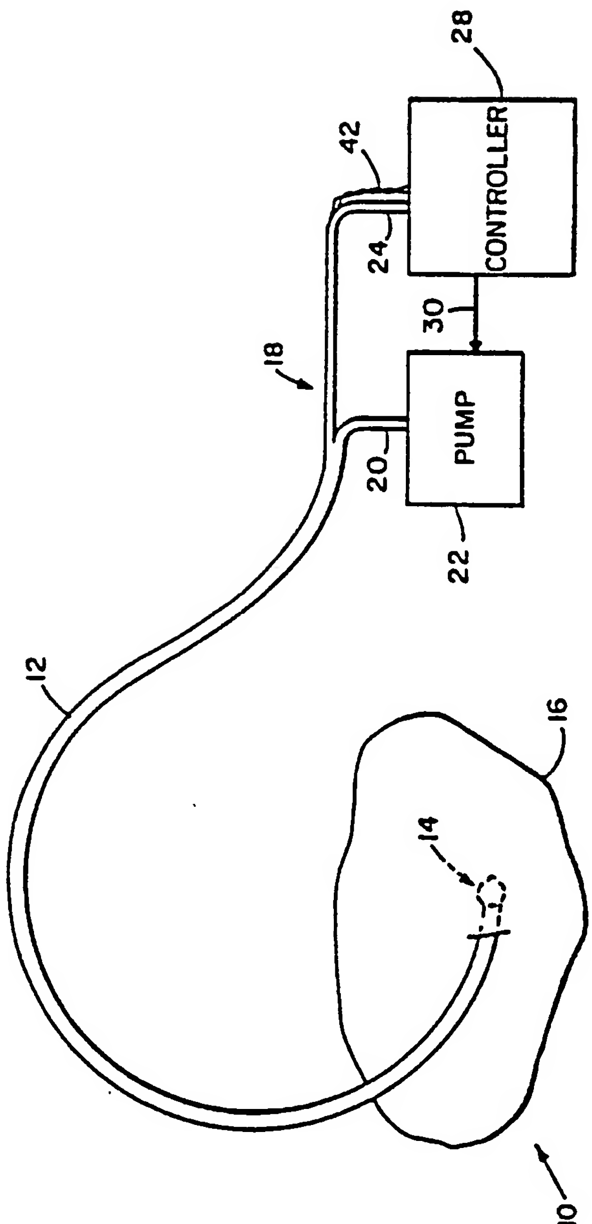
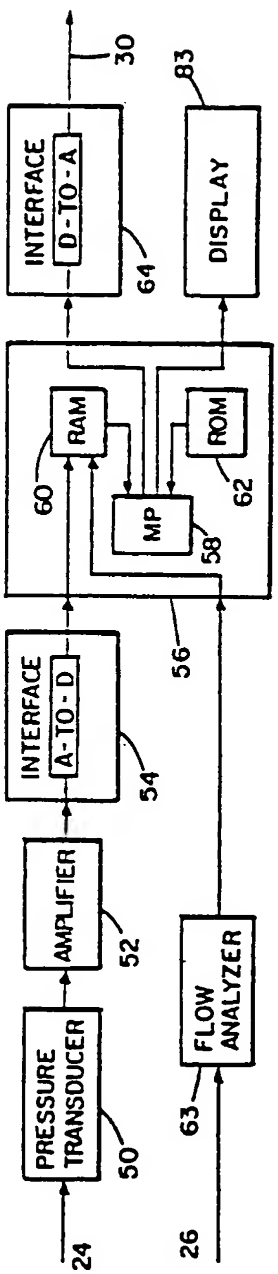

CONTROLLER
PUMP
28
42
24
30
18
20
22
12
16
14
10

FIG. 3


PRESSURE TRANSDUCER
AMPLIFIER
INTERFACE
A-TO-D
INTERFACE
D-TO-A
RAM
MP
ROM
DISPLAY
FLOW ANALYZER
24
50
52
54
56
58
60
62
63
64
83
26
30

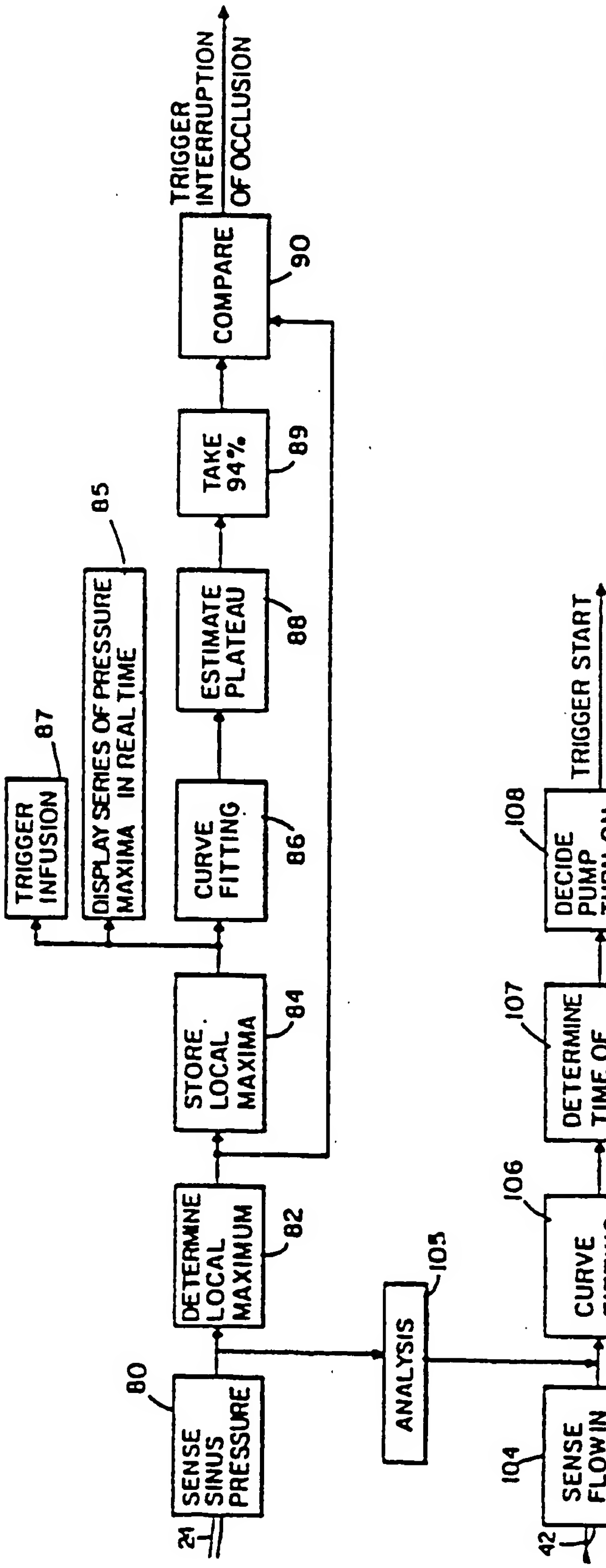

24
SENSE SINUS PRESSURE
80
DETERMINE LOCAL MAXIMUM
82
STORE LOCAL MAXIMA
84
TRIGGER INFUSION
87
DISPLAY SERIES OF PRESSURE MAXIMA IN REAL TIME
85
CURVE FITTING
86
ESTIMATE PLATEAU
88
TAKE 94%
89
COMPARE
90
TRIGGER INTERRUPTION OF OCCLUSION
ANALYSIS
105
42
SENSE FLOW IN SINUS
104
CURVE FITTING
106
DETERMINE TIME OF PEAK
107
DECIDE PUMP TURN-ON TIME
108
TRIGGER START OF OCCLUSION

FIG. 1A

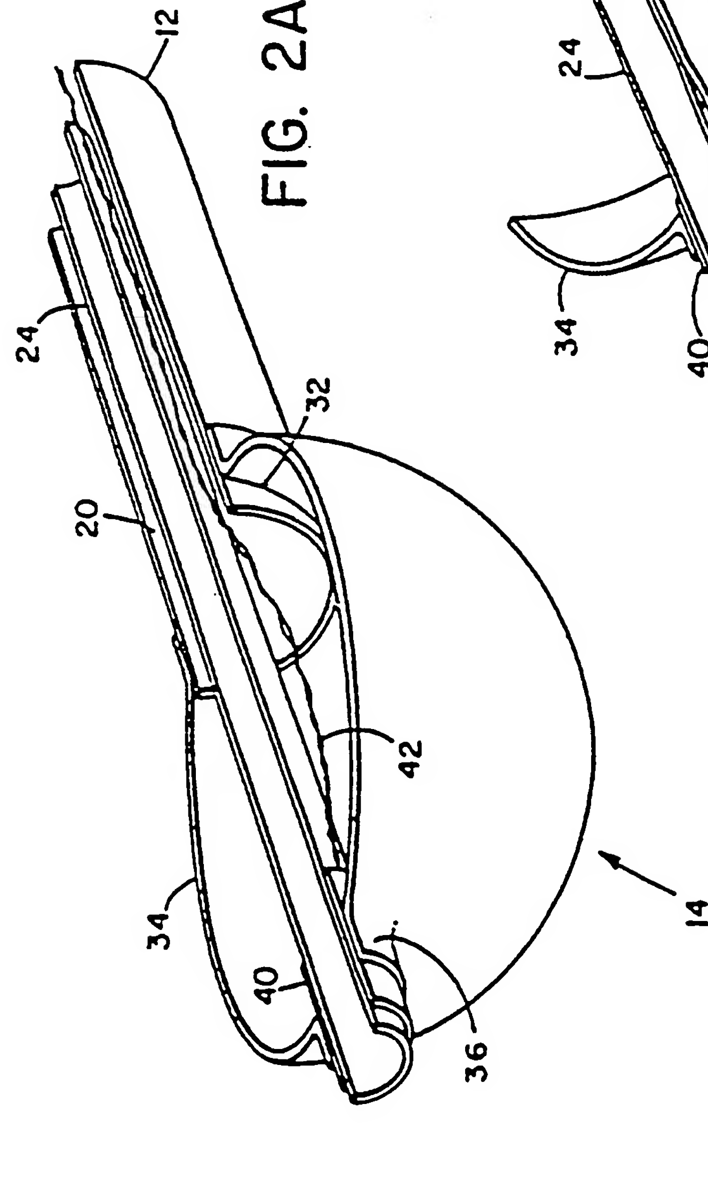


FIG. 2A

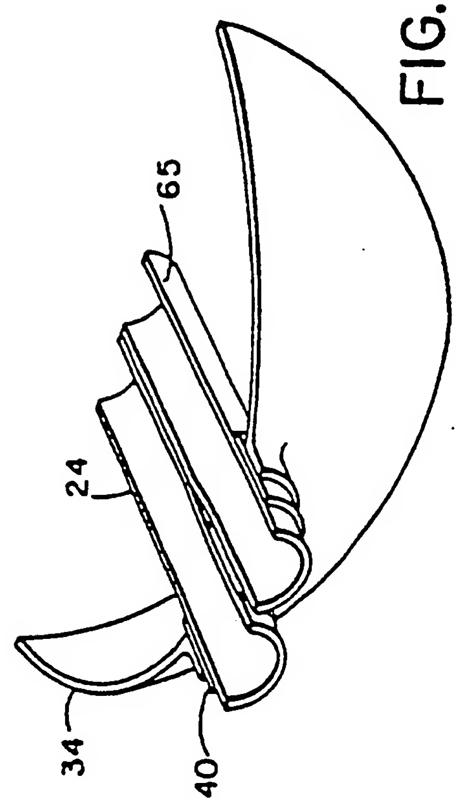


FIG. 2B

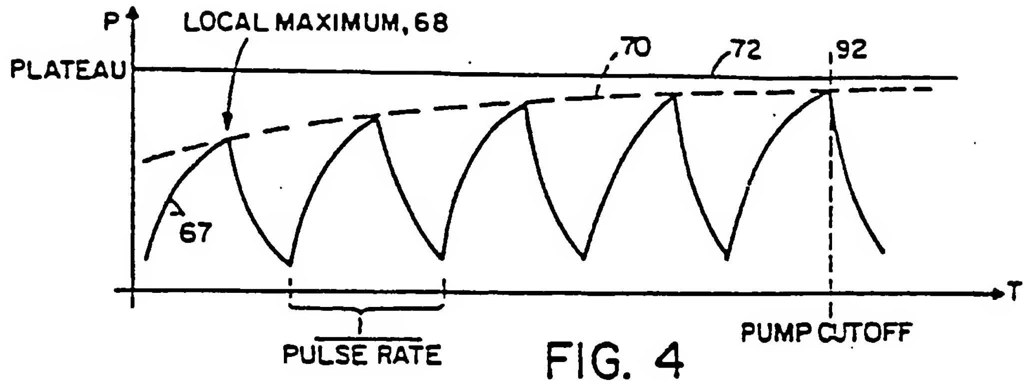


FIG. 4

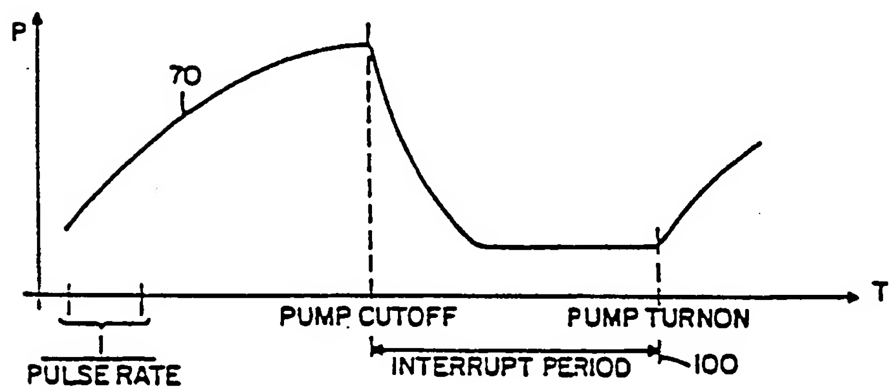


FIG. 5

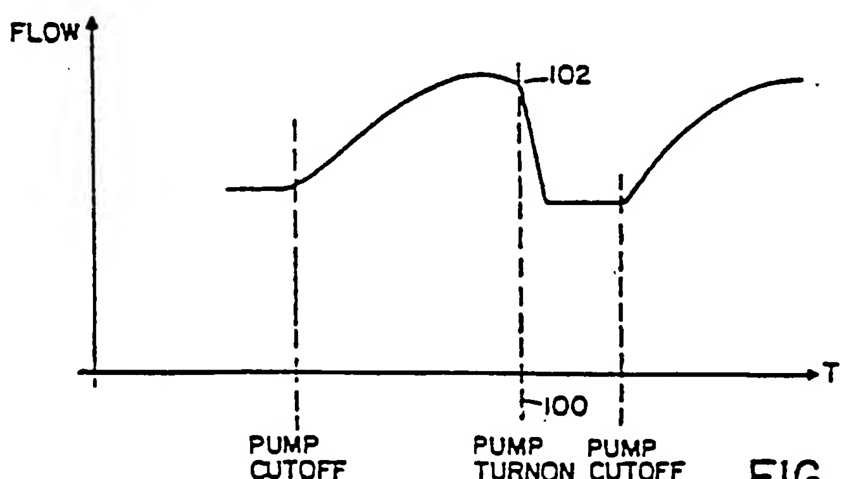


FIG. 6

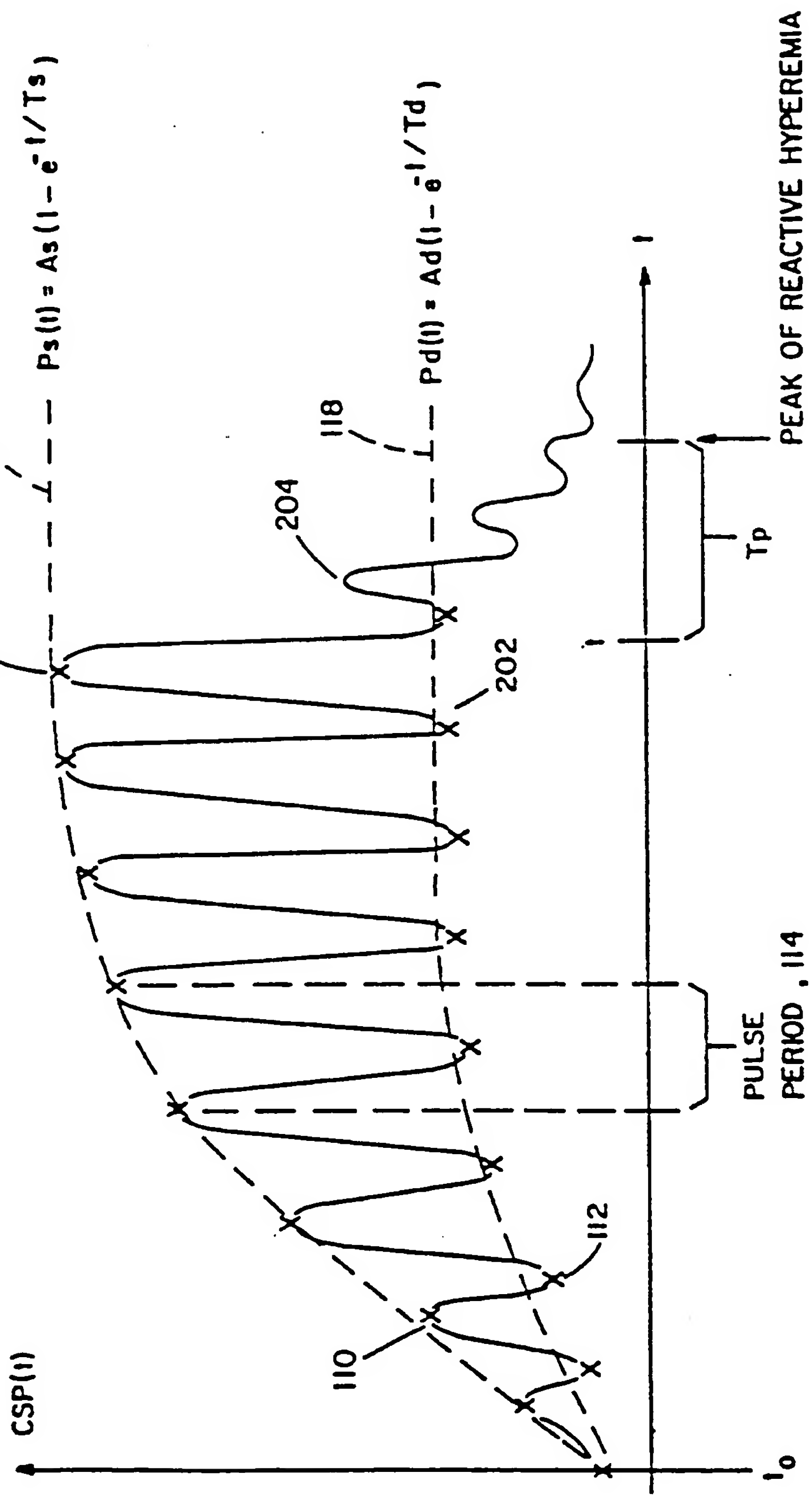

CSP(t)
110
112
116
118
Ps(t) = As(1 - e^-t/Ts)
Pd(t) = Ad(1 - e^-t/Td)
206
204
202
PULSE
PERIOD , 114
Tp
PEAK OF REACTIVE HYPEREMIA
t
t0

FIG 7

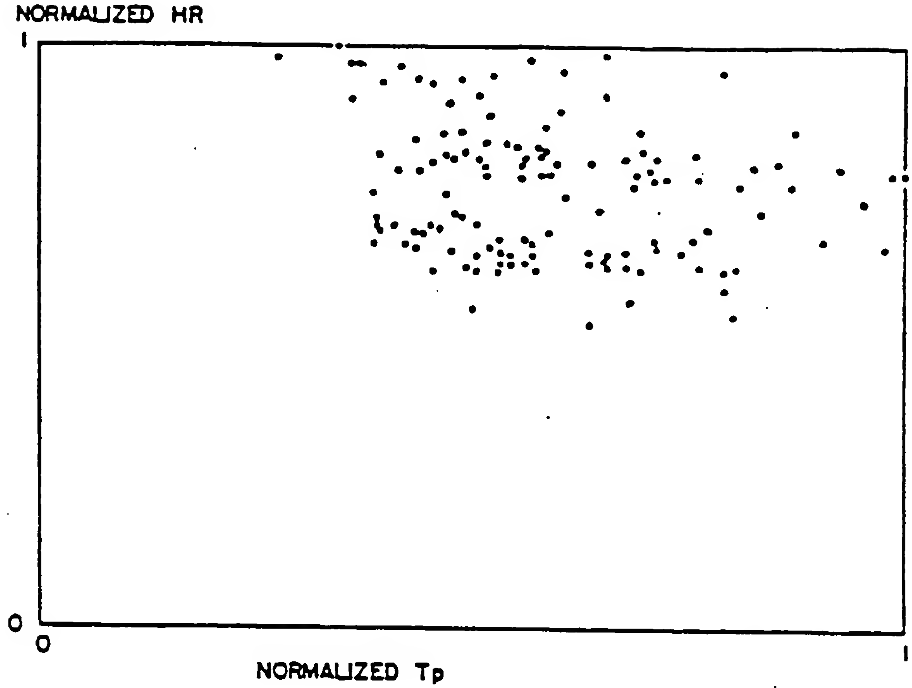

NORMALIZED HR
1
0
0
1
NORMALIZED Tp

FIG 8

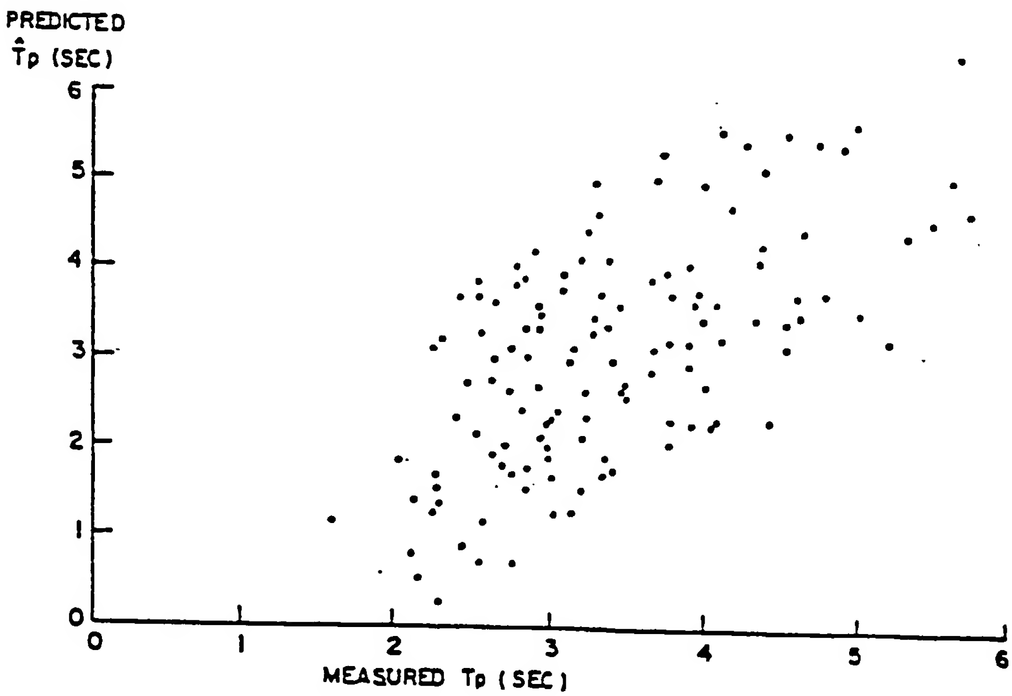

PREDICTED
$\hat{T}p$ (SEC)
6
5
4
3
2
1
0
0
1
2
3
4
5
6
MEASURED Tp (SEC)

FIG 17

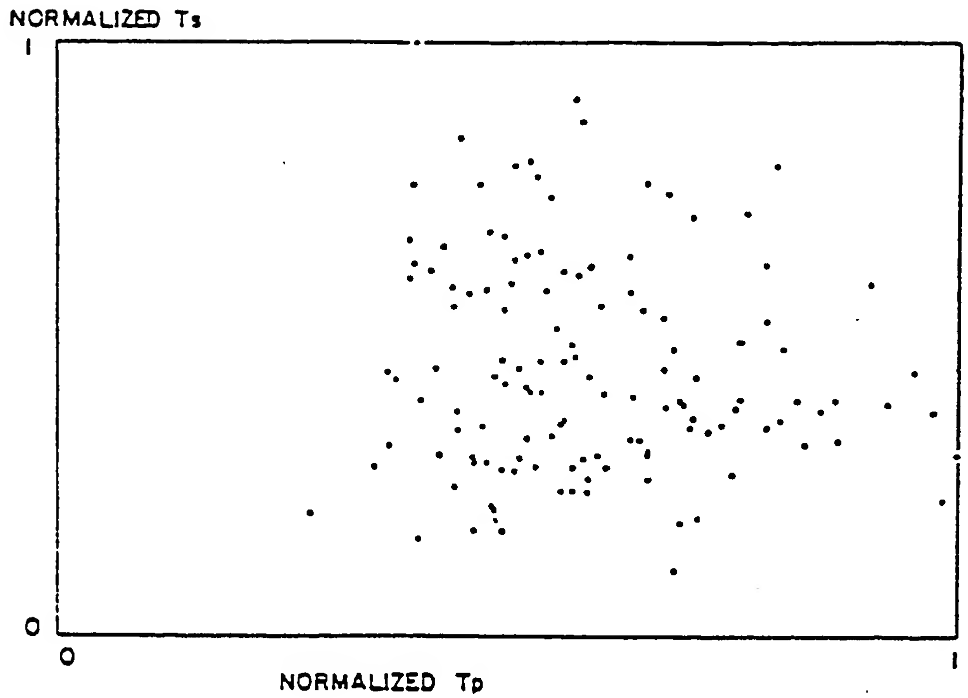

NORMALIZED Ts
1
0
0
NORMALIZED Tp
1

FIG 9

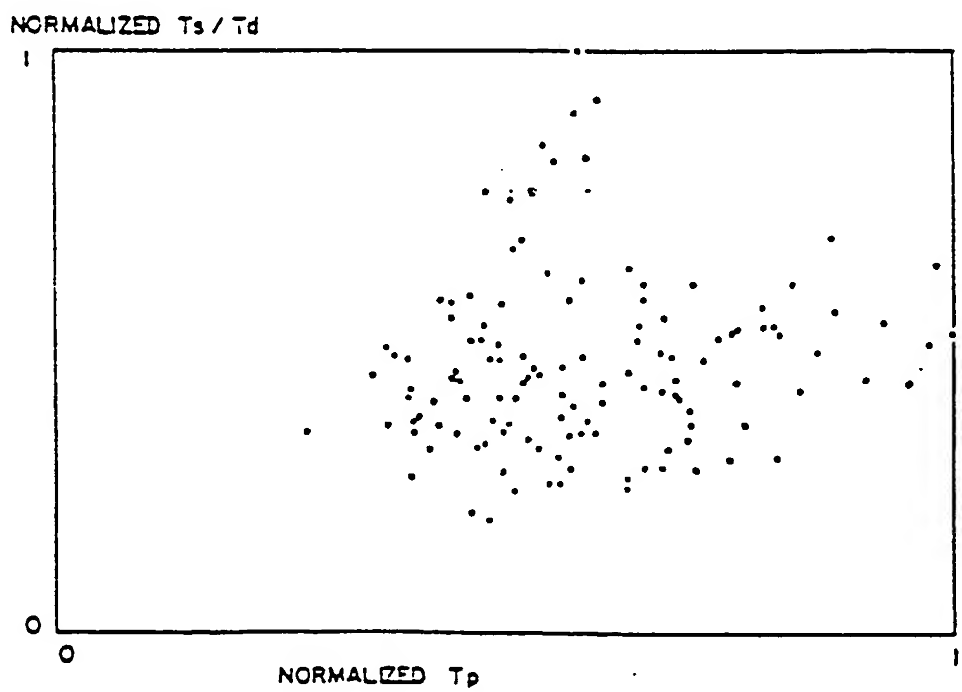

NORMALIZED Ts / Td
1
0
0
NORMALIZED Tp
1

FIG 10

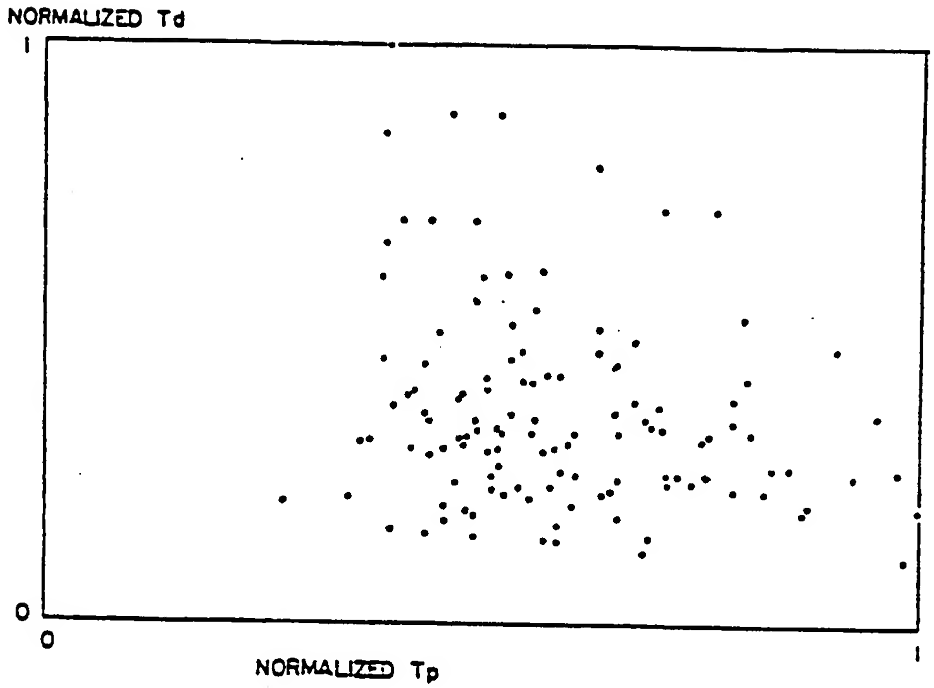

NORMALIZED Td
1
0
0
NORMALIZED Tp
1

FIG 11

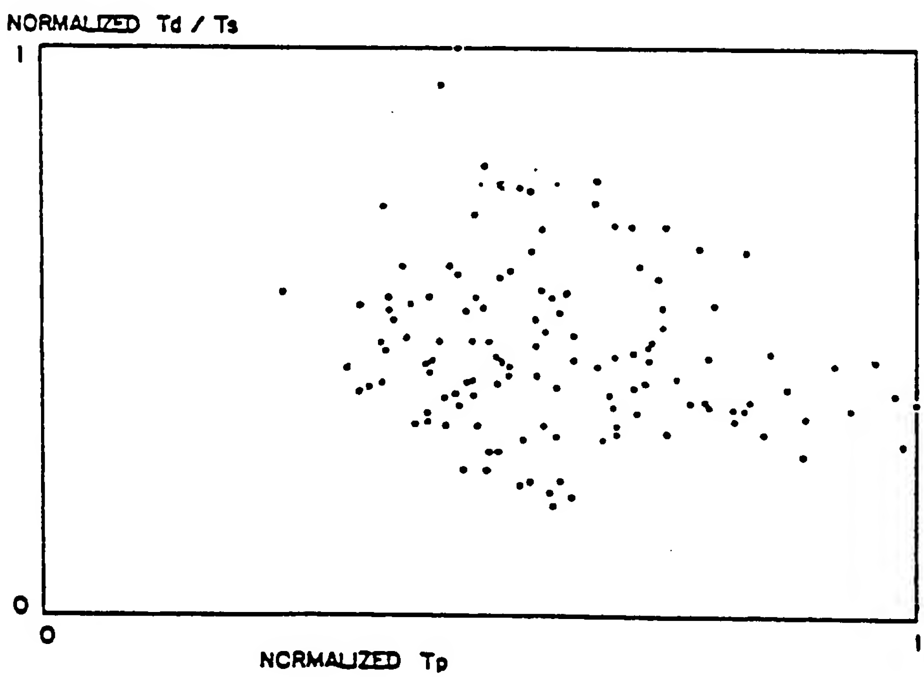

NORMALIZED Td / Ts
1
0
0
NORMALIZED Tp
1

FIG 12

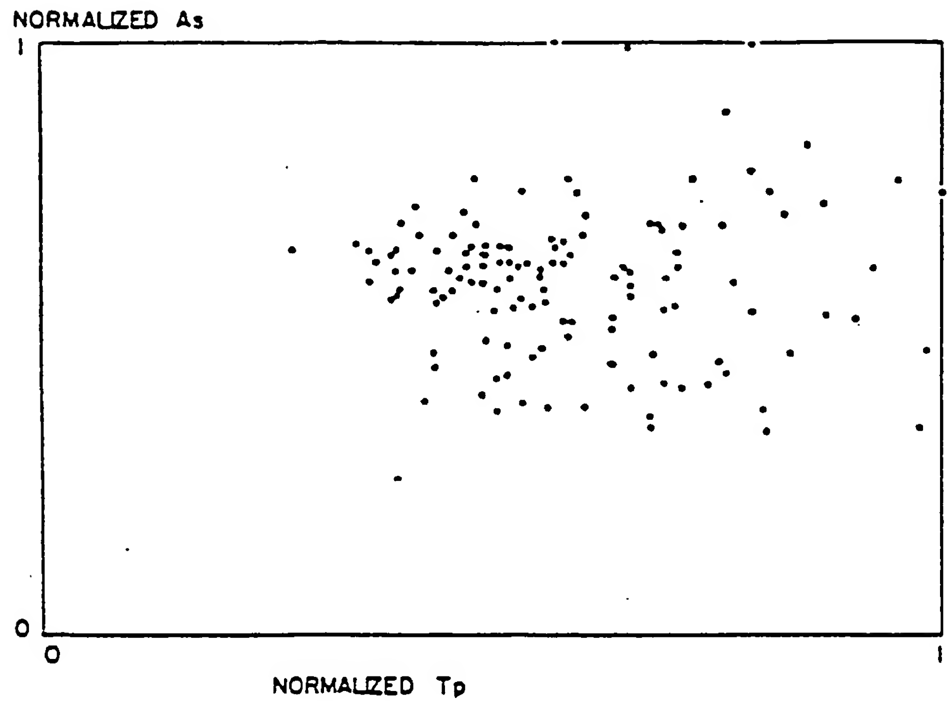

NORMALIZED As
1
0
0
1
NORMALIZED Tp

FIG 13

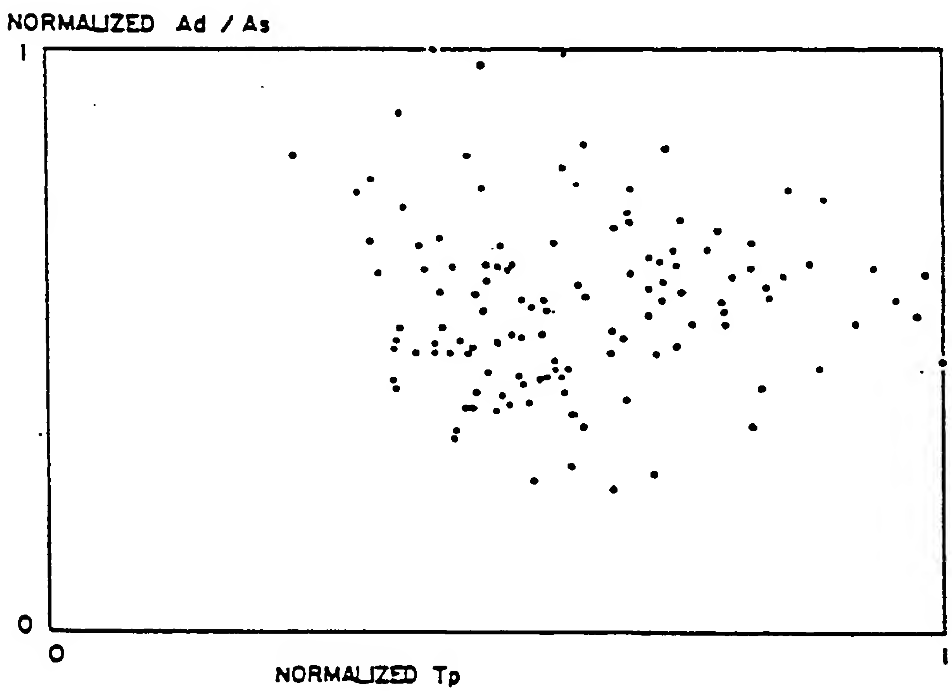

NORMALIZED Ad / As
1
0
0
1
NORMALIZED Tp

FIG 14

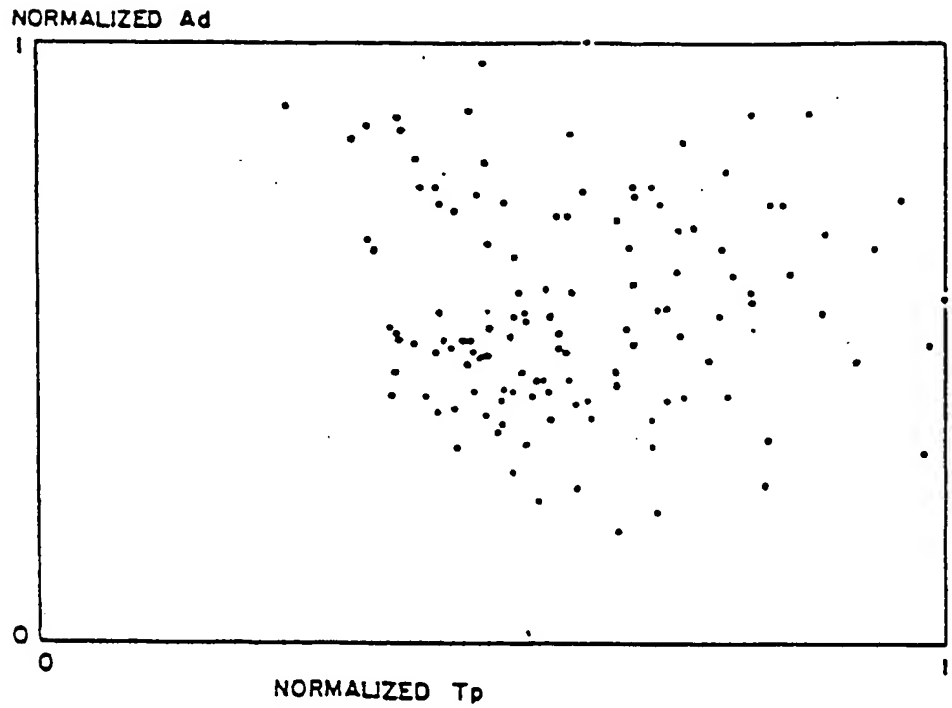

NORMALIZED Ad
1
0
0
NORMALIZED Tp
1

FIG 15

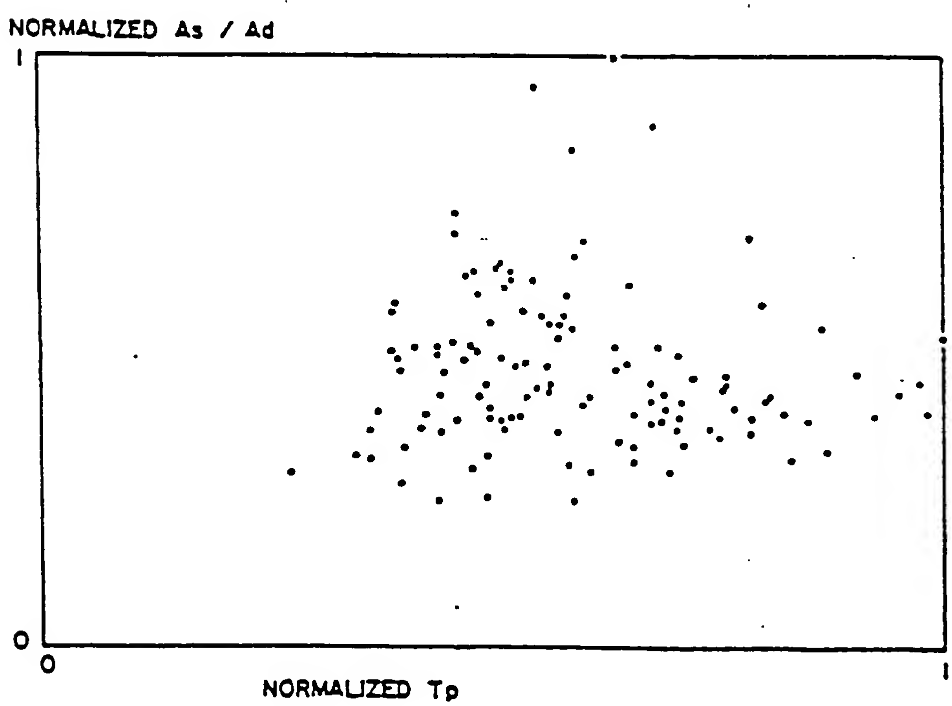

NORMALIZED As / Ad
1
0
0
NORMALIZED Tp
1

FIG 16

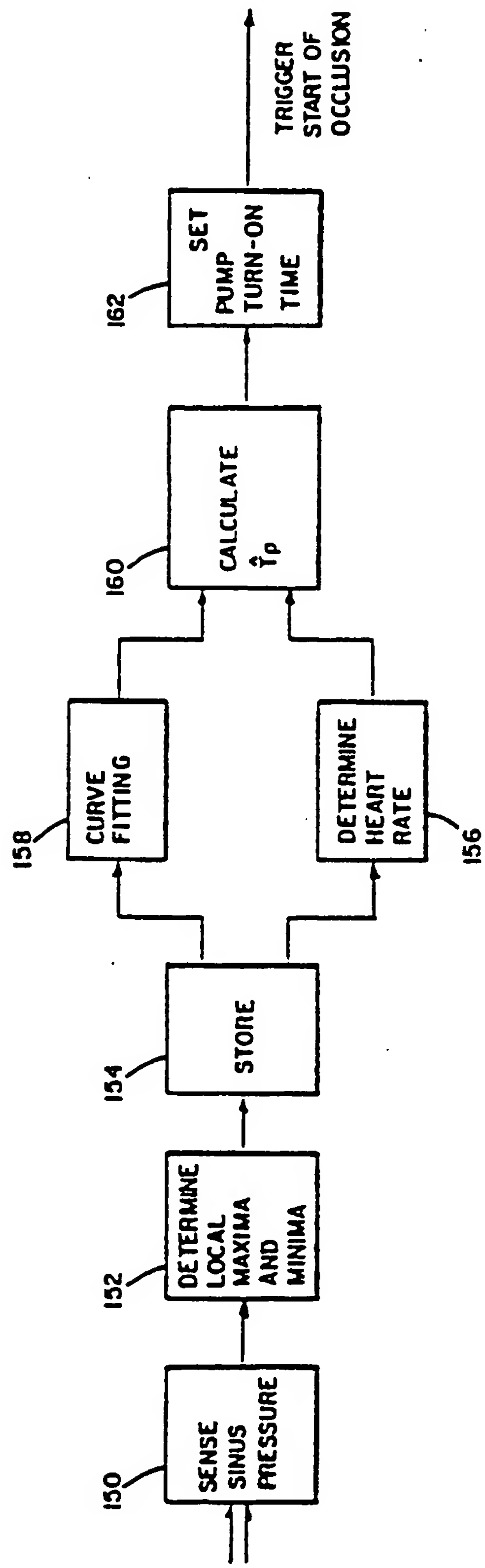

150
SENSE SINUS PRESSURE
152
DETERMINE LOCAL MAXIMA AND MINIMA
154
STORE
158
CURVE FITTING
156
DETERMINE HEART RATE
160
CALCULATE $\hat{T}_p$
162
SET PUMP TURN-ON TIME
TRIGGER START OF OCCLUSION

FIG 18

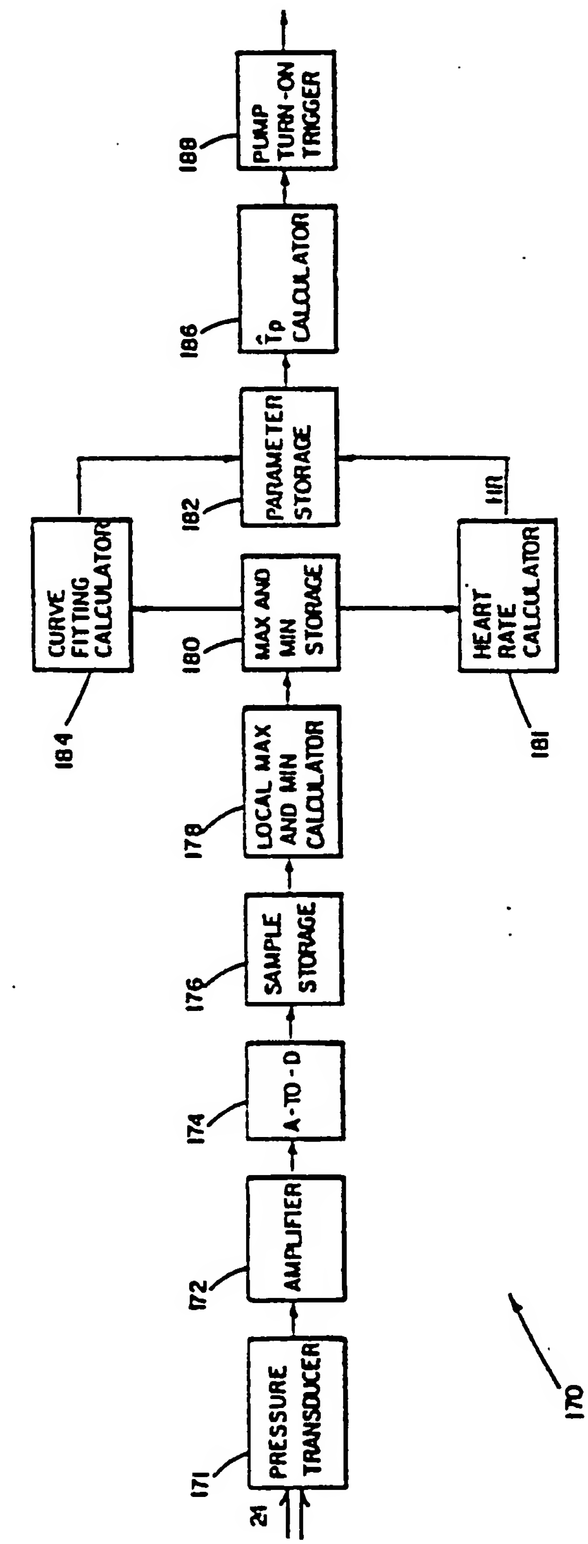

21
171
PRESSURE TRANSDUCER
172
AMPLIFIER
174
A-TO-D
176
SAMPLE STORAGE
178
LOCAL MAX AND MIN CALCULATOR
180
MAX AND MIN STORAGE
184
CURVE FITTING CALCULATOR
181
HEART RATE CALCULATOR
HR
182
PARAMETER STORAGE
186
$\hat{T}_P$ CALCULATOR
188
PUMP TURN-ON TRIGGER
170

FIG 19